

# (12) United States Patent

### Narasimhan et al.

#### US 10,874,737 B2 (10) **Patent No.:**

#### (45) Date of Patent: Dec. 29, 2020

#### (54) INFLUENZA NANOVACCINE

(71) Applicants: Iowa State University Research Foundation, Inc., Ames, IA (US): University of Iowa Research Foundation, Iowa City, IA (US)

(72) Inventors: Balaji Narasimhan, Ames, IA (US); Kathleen A. Ross, Ames, IA (US); Kevin L. Legge, Iowa City, IA (US); Thomas J. Waldschmidt, Iowa City, IA (US)

(73) Assignees: Iowa State University Research Foundation, Inc., Ames, IA (US); University of Iowa Research Foundation, Iowa City, IA (US)

(\*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: 16/370,444 Mar. 29, 2019

#### (65)**Prior Publication Data**

US 2019/0365887 A1 Dec. 5, 2019

## Related U.S. Application Data

- (60) Provisional application No. 62/681,447, filed on Jun. 6, 2018, provisional application No. 62/679,330, filed on Jun. 1, 2018.
- (51) **Int. Cl.** A61K 39/39 (2006.01)A61P 31/16 (2006.01)A61K 9/14 (2006.01)A61K 39/145 (2006.01)A61K 9/51 (2006.01)A61K 39/00 (2006.01)

(52) U.S. Cl.

(22)

Filed:

CPC ...... A61K 39/39 (2013.01); A61K 9/14 (2013.01); A61K 9/51 (2013.01); A61K 39/145 (2013.01); A61P 31/16 (2018.01); A61K 2039/525 (2013.01); A61K 2039/6093 (2013.01)

### (58) Field of Classification Search

See application file for complete search history.

#### (56)References Cited

#### U.S. PATENT DOCUMENTS

5,762,939	Α	6/1998	Smith et al.
6,475,995	B1	11/2002	Roy et al.
7,285,289			Nagy et al.
2008/0160089	A1	7/2008	Vitiello et al.
2010/0285135	A1	11/2010	Wendorf et al.
2018/0243228	$\mathbf{A}1$	8/2018	Gourapura et al.

### OTHER PUBLICATIONS

Lauster et al., Multivalent Peptide-Nanoparticle Conjugates for Influenza-Virus Inhibition, 2017, Angew. Chem. Int. Ed., vol. 56, pp. 5931-5936.\*

Hu et al., Multi-antigen avian influenza a (H7N9) virus-like particles: particulate characterizations and immunogenicity evaluation in murine and avian models, 2017, BMC Biotechnology, vol. 17, No. 2, pp. 1-12.\*

Wafa et al., The Effect of Polyanhydride Chemistry in Particlebased Cancer Vaccines on the Magnitude of the Antitumor Immune Response, 2017, Acta Biomater., vol. 50, pp. 417-427.\*

Ross et al., Structural and antigenic stability of H5N1 hemagglutinin trimer upon release from polyanhydride nanoparticles, 2014, Journal Biomed Mater Res Part A, vol. 102A, pp. 4161-4168.\*

Goodman et al., "Adaptive Immunity and Protection Generated by Nanoparticle-based Vaccination against Influenza Virus," Front. Bioeng. Biotechnol. Conference Abstract: 10th World Biomaterials Congress, Montréal, Canada, May 17-May 22, 2016, 2pgs.

Haughney et al., "Effect of Nanovaccine Chemistry on Humoral Immune Response Kinetics and Maturation," Nanoscale, 6(22):13770-13778, Nov. 2014.

Kim et al., "Antigen Persistence and the Control of Local T Cell Memory by Migrant Respiratory Dendritic Cells After Acute Virus Infection," J Exp Med., 207(6):1161-1172, Jun. 2010.

Kipper et al., "Single Dose Vaccine Based on Biodegradable Polyanhydride Microspheres Can Modulate Immune Response Mechanism," J Biomed Mater Res A., 76(4):798-810, Mar. 2006.

Narasimhan, B., "Pathogen Mimicking Nanovaccine Platform Technology: A New Paradigm," Nat'l Univ of Singapore, Department of Microbiology & Immunology Programme Seminar Series, Aug. 15, 2013, 1 pg.

Plotkin, S.A., "Vaccines: Correlates of Vaccine-Induced Immunity," Clin Infect Dis., 47(3):401-409, Aug. 2008.

Ross et a., "Combination Nanovaccine Demonstrates Synergistic Enhancement in Efficacy against Influenza," ACS Biomater. Sci. Eng., 2(3):368-374, Jan. 2016.

Ross et al., "Hemagglutinin-Based Polyanhydride Nanovaccines against H5N1 Influenza Elicit Protective Virus Neutralizing Titers and Cell-Mediated Immunity," Int J Nanomedicine, 10:229-243, Dec. 2014.

Ross et al., "(526e) Intranasal Nanovaccine Provides Protection Against Homologous and Heterologous Influenza Virus," accessed on the internet at https://www.aiche.org/conferences/aiche-annualmeeting/2017/proceeding/paper/526e-intranasal-nanovaccine-providesprotection-against-homologous-and-heterologous-influenza-virus, retrieved Mar. 30, 2018, 3pgs.

Ross, K., "Synthetic Nanoparticle-based Vaccines against Respiratory Pathogens," Iowa State University, Dissertation, 2013.

Torres et al., "Synthesis and Characterization of Novel Polyanhydrides with Tailored Erosion Mechanisms," J Biomed Mater Res A., 76(1):102-110, Jan. 2006.

### (Continued)

Primary Examiner — Benjamin P Blumel (74) Attorney, Agent, or Firm — Haukaas Fortius PLLC; Michael H. Haukaas

#### (57)ABSTRACT

Immunogenic compositions and methods of using them include a biodegradable or bioerodible polyanhydride nanoparticle comprising 1,8-bis(p-carboxyphenoxy)-3,6-dioxaoctane (CPTEG) and 1,6-bis(p-carboxyphenoxy)hexane (CPH) copolymers, an immunogenic protein of an Influenza Virus and an adjuvant entrapped within an interior of the nanoparticle, and an excipient. The immunogenic composition may be administered to a subject to confer both local and systemic immunity to the Influenza Virus.

### 20 Claims, 24 Drawing Sheets